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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/605,452	09/30/2003	William G. Kerr	1372.79.PRC	2451

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/605,452	KERR ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,32,35 and 39-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29,32,35 and 39-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of August 9, 2005 on January 12, 2006. Claims 29 and 35 are amended. Claims 42-51 are new. Claims 1-28, 30-31, 33-34, 36-38 are cancelled.

Claims 29, 32, 35, 39-51 are under consideration.

Information Disclosure Statement

Applicant filed an IDS on January 12, 2006. The IDS has been considered.

Specification

Applicant notes that an amendment to the specification, filed May 17, 2005 has removed a hyperlink. The Examiner acknowledges the amendment.

Applicant has amended the specification to provide SEQ ID NOs. to Figures 2, 3, and 7. It is also noted that in the amendment to the specification, Applicant has included a description of the sequences.

Withdrawn Rejections

35 U.S.C. § 112, 1st parag. Written Description

Applicant's arguments, see pages 15-19 of Applicant's response, filed January 12, 2006, with respect to the rejection of claims 29-41 have been fully considered and are persuasive. Applicant indicates that the art teaches that RNAi was well known by 2001, which is before Applicant's filing date. The

rejection of claims 29, 32, 35, 39, 40, 41 has been withdrawn. Claims 30-31, 33-34, 36-38 are cancelled and thus he rejection regarding these claims is moot.

Maintained Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29, 32, 35, 39-41 remain rejected and claims 42-51 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record, August 9, 2005.

Response to Arguments

Applicant's arguments filed Janurary 12, 2006 have been fully considered and are persuasive in part.

Applicant's argument (Applicant's response, pages 10-12) that the specification and art provide guidance for an artisan to practice the claimed invention of reducing s-SHIP or SIP-110 expression in mouse or human stem cells, wherein said mouse or human stem cells proliferate and/or differentiate is not persuasive. The issue at hand is whether the artisan had guidance to arrive at the claimed invention. That is, would an artisan have known what

phenotype(s) would result in any mouse or human stem cells following administration of s-SHIP or SIP-110 shRNA (Office Action, pages 9-10). At the time of filing, neither the art nor specification provides this guidance. It should be made clear that it is not enough to say that any stem cell would have differentiated in to a more specific cell type or that there is the likelihood that reduction of s-SHIP or SIP-110 results in proliferation in some subsets of stem cells. The point is, that at the time of filing, the art of factors involved in differentiation and proliferation in stem cells and the function of s-SHIP/SIP-110 in cells was not well known that an artisan could not predictably arrive at the claimed invention. As such, an artisan is not enabled to practice the claimed invention.

Applicant provides an unpublished manuscript (Exhibit B) that indicates that Dr. Kerr's laboratory has found that a loss-of-function mutation in s-SHIP results in expansion of the hematopoietic stem cell (HSC) compartment *in vivo* (Applicant's response, page 10). While Applicant provides this post-filing teaching, the teaching is different from that of the claimed invention as the claimed invention is drawn to RNAi and the teaching is drawn to a knockout. An artisan cannot predict what level of RNAi inhibition is required such that a phenotype of expansion would occur. Further, the teaching does not overcome the fact that at the time of filing, an artisan could not predict that HSC would have resulted in proliferation upon treatment with s-SHIP/SIP-110 mRNA. Nothing in the art at the time of filing provides guidance that there was a relationship between HSC and s-SHIP/SIP-110 that an artisan could reasonably expect that

the HSC cells would have proliferated when endogenous levels of s-SHIP/SIP-110 were reduced. As stated in In re Glass, 181 USPQ 31, (CCPA 1974), if a disclosure is insufficient as of the time it is filed, it cannot be made sufficient, while the application is still pending by later publications which add to the knowledge of the art so that the disclosure, supplemented by such publications, would suffice to enable the practice of the invention. Instead, sufficiency must be judged as of the filing date. The fact that the specific protocol is not disclosed in the specification indicates that the specification does not support the claims as filed, but instead reflects further critical information that is essential for the artisan to practice the invention. As such, the specification and art do not enable an artisan to practice the claimed invention for HSC and proliferation.

Applicant indicate that claims 41 and 48 only require that the cells are induced to differentiate and that methods of differentiating primitive cells were well known at the time of filing (Applicant's emphasis, Applicant's response, page 10-11). Applicant indicates references (Shah et al., 1996, Cell, 85: 331-343; White et al., 2001, Neuron, 29: 57-71; Watt et al., 2000, Science, 287: 1427-1430; Lee et al., 2000, Nature Biotechnology, 18: 675-679; Lumelsky et al., 2001, Science, 292: 1389-1394; and Appendix D of Exhibit C (Stem Cells: Scientific Progress and Future Research Directions)) to show that at the time of filing, the art teaches that the methods used to differentiate cells were well known. In response, it is reiterated that it is not enough to say that treating any stem cell with s-SHIP or SIP-110 shRNA would likely result in the cell exhibiting differentiation and/or proliferation. The issue at hand is that an ES cell or any

stem cell has the potential to differentiate or proliferate into many different cell types; however, how s-SHIP has a role in causing an ES cell or a stem cell to differentiate or proliferate is not readily apparent at the time of filing. Regarding the citations of Shah et al., 1996, White et al., 2001, Watt et al., 2000, Lee et al., 2000, Lumelsky et al., 2001, and Appendix D of Stem Cells: Scientific Progress and Future Research Directions, while these teachings provide guidance for differentiation/proliferation in a variety of stem cells, none of these references indicate that there is a role of s-SHIP or SIP-110 in differentiation/proliferation in these cells. As such, these teachings in the art do not enable the claimed invention.

In response to the Examiner indicating that the instant application does not teach that administration of s-SHIP or SIP-110 shRNA results in proliferation of other stem cells such as neuronal stem cells and osteoblastic stem cells, Applicant indicates that Dr. Kerr's laboratory has found that proliferation of HSC proliferation increases following s-SHIP deficiency in these cells and it is reasonable to conclude that this may also be the case in other stem cells that express SHIP or SIP-110 (Applicant's response, pages 11-12). While Applicant provides this assertion, the Examiner does not find it persuasive because the art teaches that at the time of filing, the relationship between stem cells, proliferation/ differentiation, and s-SHIP/SIP-110 was not known and thus, an artisan cannot reasonably practice the claimed invention. Regarding the assertion that post-filing art indicates that the claimed invention is enabled for

other embodiments of stem cells, this is not persuasive as the disclosure must be enabled at the time of filing.

Regarding the issue that the art at the time of filing teaches an artisan how to make and use shRNA (Applicant's response, pages 12-14), the Examiner finds the Applicant's argument persuasive. This is because in 2001, before the time the Application was filed, the art teaches the steps needed to make shRNA for any gene. As such, the rejection regarding this issue is withdrawn.

Thus, for the reasons described above, the rejection of claims 29, 32, 35, 39-51 remain.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history

information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WE...
PRIMARY EXAMINER